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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/608,463 | 06/27/2003 | James W. Ryan | JR-10,003-US | 6428 |

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| EXAMINER | |
|---|---|
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| **ART UNIT** | **PAPER NUMBER** |
| 1652 | |

DATE MAILED: 08/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/608,463 | RYAN, JAMES W. | |
| | Examiner | Art Unit | |
| | Elizabeth Slobodyansky, PhD | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *7,8,10,12,14-18,20,22-28 and 30-32* is/are pending in the application.

4a) Of the above claim(s) *8,12,14,22,23 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,10,15-18,20,24-28,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

The amendment filed June 8, 2006 amending claim 7 and adding claim 32 has been entered.

Claims 7, 8, 10, 12, 14-18, 20, 22-28 and 30-32 are pending.

Claims 7, 10, 15-18, 20, 24-28, 30 and 31 are under consideration. Claims 8, 12, 14, 22 and 23 have been previously withdrawn.

### *Election/Restrictions*

Newly submitted claim 32 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

While claim 7 and claim 32 are related as product and process of use, these claims are drawn to distinct inventions as explained in the Office actions mailed May 6, 2004 and May 25, 2005.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 32 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

### *Claim Objections*

Claim 7, with dependent claims 10, 15-18, 20, 26, 27, 28, 30, 31, are objected to as reciting the non-elected subject matter of 5' and 3' non-coding regions and introns. Appropriate correction is required.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7, 10, 15-18, 20, 24-28, 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muzny et al. in view of Vogelstein et al.

Muzny et al. (GenBank accession AC025423, March 9, 2000, cited on form PTO-892 mailed 12/1/04) teach the sequence of human chromosome 12 comprising the sequence of SEQ ID NO:4. Said sequence is of at least 20 nucleotides and is a contiguous exon-intron or intron-exon region of SEQ ID NO:4.

Vogelstein et al. (US Patent 5,411,860, GenBank accession NM_002392, cited on form PTO-892 mailed 12/1/04) teach cloning, functional expression and chromosomal localization of human mouse double minute (MDM2) homolog. They teach cDNA (SEQ ID NO:1) encoding human MDM2 homolog (SEQ ID NO:2) that is 100% identical to the human MDM2 homolog of the instant invention (SEQ ID NO:2). Using a labeled probe, they localized the gene encoding said human MDM2 homolog to chromosome 12q12-14 (column 5, lines 2-13; the description of SEQ ID NO:1 in the Sequence Listing). SEQ ID NO:1 comprises 5' non-coding region consisting of nucleotides 1-296. The elected

species of 41739-41738 correspond to exon-intron junction within the genomic DNA corresponding to said 5' non-coding region.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use said cDNA to identify the genomic DNA that encodes the human MDM2 homolog of SEQ ID NO:2 on chromosome 12q12-14. The motivation is provided by Vogelstein et al. who teach that it binds to oncogene p53 and is diagnostic of tumorogenesis. The state of the art provides various techniques for obtaining genomic DNA using cDNA probes that are usually labeled. The comparison of genomic and cDNA would result in the identification of regions comprising exon-intron and intron-exon junctions within coding and non-coding regions. One of ordinary skill in the art would have been motivated to use said non-coding regions or fragments thereof of at least 20 nucleotides and up to 5000 or 51039 nucleotides (the entire length of SEQ ID NO:4) nucleotides for detecting splice variants of chromosome 12q12-14 from genomic nucleotide samples from an individual, for example. As a matter of convenience a non-coding region such as an exon-intron or intron-exon region or fragments thereof can be present in a kit or on a solid support. Further, said support can be a microarray according to a customary use of nucleic acid molecules in the art.

***Response to Arguments***

Applicant's arguments filed June 8, 2006 have been fully considered but they are not persuasive.

The 112, 2$^{nd}$ paragraph rejection is withdrawn in view of the amendment.

With regard to the objection of claim 7, Applicant argues "Claim 7 has been amended accordingly to recite that it the region additionally is selected from the group consisting of "a contiguous exon-intron region" and "contiguous intron-exon region", both of which encompass the elected species, a splice junction" (Remarks, page 6; page 9, penultimate paragraph). This is not persuasive because the claim still recites non-elected species such as an intron, etc., for example.

With regard to the 103(a) rejection, Applicant argues that "First given that Muzny only discloses the sequence of the clone AC025423 but does not suggest that SEQ ID NO:4 or any other gene could be located on this clone and given that Vogelstein only provides a rough location for the MDM2 gene and the cDNA sequence which only constitutes a very small portion of the genomic sequence, one of ordinary skill in the art as of the priority date would not have had a reasonable expectation of success of obtaining the genomic sequence and subsequently the introns. At best as pointed out in the Office Action, there may have been a motivation to search the cDNA sequence against the entire genomic DNA in order to find the identical regions but not necessarily a reasonable expectation of success. However, that is not sufficient" (pages 8-9). This is not persuasive because the exact location of the gene is not necessary as long as its sequence is known as in the instant case. Further, Applicant does not explain why there is no expectation of success when finding non-coding regions using cDNA and genomic DNA was standard technique at the time of filing the current application.

As previously argued, there would not be any motivation to combine Muzny et al with Vogelstein et al. Muzny et al knew that clone AC025423 (from 1V11-61102) was from chromosome 12 but there is no evidence in the NCBI report of a sub-assignment to the p- or q-arm. Chromosome 12 is about 130 million base pairs long and is believed to contain several hundred genes (by analysis after 2001 and after the Applicant discovered the human MDM2 homologue gene). Further, there is no evidence that Muzny et al. knew whether the clone did or did not contain one or more genes and particularly whether it contained the gene encoded by SEQ ID NO:4. Vogelstein et al. placed the human MDM2 homologue gene at 12q12-14. Actually, this finding is incorrect. After the publication of Vogelstein, the gene was found to be located at 12q12-14, whereas the gene is actually several millions of base pairs away at 12q15 (see Genecard attached hereto as Appendix B). There was actually a previous disclosure stating that the MDM2 was located between 12q14.3-15 (see, for example, Andersen et al., 1996, Mammalian Genome 7:780-783 and Bureau, 1995, Genomics 28: 109-112, submitted herewith as an IDS ). However, given the conflicting locations published, one of ordinary skill in the art would not have known which location was actually correct. Clearly combining the disclosures of Muzny et al. with Vogelstein et al. would not have produced the claimed sequences, especially given Vogelstein's mistaken assignment of MDM2 to 12q12-14" (Remarks, pages 14-15). This is not persuasive because it is well

known in the art that the localization on the chromosome is often imprecise. However, one of ordinary skill in the art would have been motivated to search the cDNA sequence against the entire genomic DNA in order to find the identical regions.

Applicant further argues "First, there are a large number of sequences to choose from, the sequences contained within AC025423; the permutations and combinations are indeed significant given that the cDNA only constitutes such a minute portion (1.6%) of the AC025423 sequence" (page 10, lines 1-3). This is not persuasive because Applicants does not explain why the fact that cDNA constitutes 1.6% of the AC025423 sequence prevents finding non-coding regions in the genomic DNA. Applicants further argues relating to the Bell court "Analogously, the prior art discloses the known MDM2 cDNA and there are large numbers of possibilities as to which sequences may be the genomic sequence but no suggestion as to which possibility is indeed the genomic sequence" (page 10). This is not persuasive because Applicant does not give any example when indeed he was faced with multiple choices in identifying any non-coding region. unless said sequence is very small, it is not clear why there is a large number of sequences and not a single one.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652